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10/520,659

01/10/2006

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EXAMINER

BLAND, LAYLA D

ART UNIT

PAPER NUMBER

1623

MAIL DATE

DELIVERY MODE

02/26/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

|                              |                                      |                                       |  |
|------------------------------|--------------------------------------|---------------------------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>10/520,659 | <b>Applicant(s)</b><br>HABUCHI ET AL. |  |
|                              | <b>Examiner</b><br>LAYLA BLAND       | <b>Art Unit</b><br>1623               |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 28 December 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-4,7 and 10-12 is/are pending in the application.
- 4a) Of the above claim(s) 7 and 10-12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### DETAILED ACTION

This office action is a response to Applicant's arguments dated December 28, 2007. All prior art rejections of the previous office action are withdrawn. This action is non-final in view of the following rejections.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds wherein  $X=O$ , does not reasonably provide enablement for compounds where X is S, NH, or  $CH_2$ . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in *Wands* states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention.

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“Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations” (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

*(1) The nature of the invention and (2) the breadth of the claims:*

The claims are drawn to compounds of formula I wherein X can be O, S, NH, or CH<sub>2</sub>.

*(3) The state of the prior art and (4) the predictability or unpredictability of the art:*

Compounds of formula I wherein X is O are known in the art. Dahlgren et al. and Fraser et al. both teach such compounds, as is discussed below. However, as stated in the preface to a recent treatise:

“Most non-chemists would probably be horrified if they were to learn how many attempted syntheses fail, and how inefficient research chemists are. The ratio of successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most scientists, spend most of their time working out what went wrong, and why. Despite the many pitfalls lurking in organic synthesis, most organic chemistry textbooks and research articles do give the impression that organic reactions just proceed smoothly and that the total synthesis of complex natural products, for instance, is maybe a labor-intensive but otherwise undemanding task. In fact, most syntheses of structurally complex natural products are the result of several years of hard work by a team of chemists, with almost every step requiring careful optimization. The final synthesis usually looks quite different from that originally planned, because of

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unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even the repetition) of a synthesis usually implies will be able to appraise such work.....Chemists tend not to publish negative results, because these are, as opposed to positive results, never definite (and far too copious)....." Dorwald F. A. *Side Reactions in Organic Synthesis*, 2005, Wiley: VCH, Weinheim pg. IX of Preface.

Thus, the synthesis of compounds of formula I wherein X is S, NH, or CH<sub>2</sub> is expected to be non-trivial.

*(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:*

The specification has provided guidance for the preparation of compounds of formula I wherein X is O.

However, the specification does not provide guidance for the preparation of compounds of formula I wherein X is other than O.

*(8) The quantity of experimentation necessary:*

Considering the state of the art as discussed by the references above, particularly with regards to the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one

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skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the amendment dated August 27, 2007, claims 1 and 2 were amended to exclude a compound in which  $R^1$  and  $R^2$  are H,  $R^5$  is  $SO_3^-$ ,  $R^3$  is an acetyl group,  $R^4$  is a para-nitrophenyl group and X is O. Claim was amended to exclude a genus of compounds wherein  $R^1$ ,  $R^2$  and  $R^5$  are each independently  $SO_3^-$  or H,  $R^3$  is H, an acetyl group or  $SO_3^-$ ,  $R^4$  is a benzyl group and X is O. These are not described in the specification. See MPEP 2173.05(i): Any negative limitation or exclusionary proviso must have basis in the original disclosure. Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

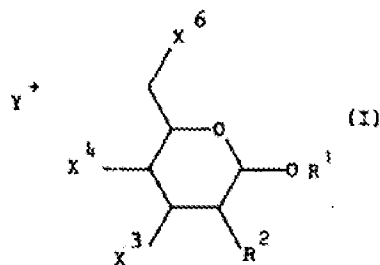
A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Dahlgren et al. (WO 97/00879, January 9, 1997, of record).

Dahlgren et al. teach compounds of the following formula:

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wherein X<sup>3</sup>, X<sup>4</sup> and X<sup>6</sup> can all be OH or SO<sub>4</sub><sup>-</sup>, R<sup>2</sup> can be OH, SO<sub>4</sub><sup>-</sup>, or substituted amine including NHAc, and R<sup>1</sup> can be hydrogen, alkyl, benzyl, amino acid, nucleotide or polypeptide. When at least one of X<sup>3</sup>, X<sup>4</sup> and X<sup>6</sup> are SO<sub>4</sub><sup>-</sup>, R<sup>2</sup> is NHAc, and R<sup>1</sup> is alkyl or hydrogen, the limitations of claim 1 are met.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Fraser et al. (The Journal of Biological Chemistry, vol. 276, No. 9, pages 6412-6419, PTO-1449 submitted January 10, 2005).

Fraser et al. teach GalNAc-4S, GalNAc-6S, and GalNAc-4S,6S [page 6417, Table I]. These compounds meet the limitations of claim 1 when R<sup>3</sup> is acetyl, X is O and R<sup>1</sup> is H.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 2-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dahlgren et al. (WO 97/00879, January 9, 1997, of record) in view of Greene et al. (Protective Groups in Organic Synthesis, Third Edition, John Wiley & Sons, Inc. 1999, of record).

Dahlgren et al. teach as set forth above.

Dahlgren et al. do not teach compounds wherein R<sup>1</sup> is an aryl group other than benzyl.

Greene et al. teach 2- and 4-picolyl ethers as protecting groups for the hydroxyl function [page 99]. They are prepared from their chlorides and can be removed by hydrogenolysis in acetic acid. Greene et al. also teach 1-pyrenylmethyl ether as a protecting group for the hydroxyl group [page 100]. It is introduced using the chloride and can be removed by methods used for benzyl ether cleavage. These are only two examples of a plethora of aryl protecting groups available for the hydroxyl group.

In the amendment dated August 27, 2007, Applicant amended claim 1 such that the particular species taught by Dahlgren et al. wherein R<sup>1</sup> is benzyl are excluded. Thus, claims 2-4 are not anticipated by Dahlgren et al. However, it would have been obvious to one of ordinary skill in the art to prepare the compounds of Dahlgren et al. using aryl protecting groups other than benzyl, such as a picolyl ether or a 1-pyrenylmethyl ether, as taught by Greene et al. These are known alternatives to the benzyl group, which was taught by Dahlgren et al. One of ordinary skill in the art could have substituted one alternative for another and could have predicted the success of the preparation, based on the teachings of Greene.



### ***Response to Arguments***

Applicant's arguments filed December 28, 2007 have been fully considered but they are not persuasive. Applicant argues that Dahlgren fails to disclose any specific or significant utility for the intermediate compounds containing a benzyl moiety and as such it would not be obvious to terminate the reaction before removal of the protecting group.

Dahlgren teaches that the mono-, di-, tri-, or tetra-sulfate esters of pentose or hexose are effective in the treatment of HIV and AIDS [see abstract]. The compounds containing a benzyl moiety (as well as compounds containing hydrogen, alkyl, amino acid, nucleotide, or polypeptide) are claimed compounds. The fact that the compounds are claimed, combined with the general teaching that sulfate esters of hexoses are effective for the treatment of HIV and AIDS, is evidence that the benzyl-containing compounds do have utility. Thus, Applicant's arguments are not persuasive.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAYLA BLAND whose telephone number is (571)272-9572. The examiner can normally be reached on M-F 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Layla Bland  
Patent Examiner  
Art Unit 1623  
February 7, 2008

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